Remarks

Upon entry of the foregoing amendment, claims 136-146, 148-172 and 174 are pending in the application, with claims 136 and 142 being the independent claims. Claims 138, 143, 157-161, and 163-170 are withdrawn. Claims 136 and 139 are sought to be amended. Claim 147 and 173 is sought to be cancelled. Support for the amendments to claims 136 and 139 may be found, *e.g.*, in the prior claims.

A Request for Continued Examination is being filed concurrently herewith. Accordingly, under 37 C.F.R. 1.114(d), the finality of the November 21, 2007 Office Action should be withdrawn and the present response entered and considered. Based on the above amendments and the following remarks, Applicant respectfully requests that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

Claim Objections

The Examiner objected to claim 147 under 37 C.F.R. 1.75(c) as allegedly of being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant respectfully traverses this objection.

Solely to advance prosecution and not in acquiescence to the Examiner's objection, Applicant has cancelled claim 147.

Rejections under 35 U.S.C. § 112, second paragraph

The Examiner rejected claim 137 as allegedly indefinite. Specifically, the Examiner alleged that dependent claim 137 is indefinite for reciting species of target specific linkers that are not nucleic acids while claim 136 has been amended to limit the target specific linker to a nucleic acid. Applicant respectfully traverses the rejection.

Under 35 U.S.C. § 112, fourth paragraph:

> a claim in dependent form shall contain a reference to a claim previously set forth and then specify a further limitation of the subject matter claimed. A claim in dependent form shall be construed to incorporate by reference all the limitations of the claim to which it refers.

Part (b) of claim 136 recites "a target-specific linker on at least the 3' or 5' end of one strand *with the proviso that when the target specific linker is a nucleic acid, the linker comprises a single-stranded overhang region of 5 to 40 nucleotides*." Thus, the target specific linker in claim 136 is not limited solely to nucleic acids, only the size of the overhang is limited when the linker is a nucleic acid. Claim 137 incorporates all limitations of claim 136 and further specifies that the target specific linker is selected from a group of species recited in the claim. While Applicant has elected the species DNA as the target specific linker, the Examiner should consider additional species if a generic claim is found to be allowable. Of course, when the species in claim 137 is a nucleic acid, the linker comprises a single-stranded overhang region of 5 to 40 nucleotides, in accordance with the requirements of 35 U.S.C. 112, fourth paragraph.

Applicant therefore submits that the claims are not indefinite and respectfully requests that the Examiner reconsider and withdraw the rejection

The Examiner further rejected claim 149 for recitation of "said oligonucleotide" alleging that it is unclear to which oligonucleotide the "said" oligonucleotide is referring to. Applicant respectfully traverses this rejection.

Solely to advance prosecution, and not in acquiescence to the Examiner's rejection, Applicant has amended claim 149 to recite "the oligonucleotide(s) of any of parts (a)(i), (a)(ii) or (a)(iii)."

Accordingly, Applicant respectfully requests that the Examiner reconsider and withdraw the rejection.

Rejections under 35 U.S.C. § 112, second paragraph

The Examiner rejected claim 173 under 35 U.S.C. 112, first paragraph as allegedly failing to comply with the written description requirement. Applicant respectfully traverses this rejection.

Solely to advance prosecution, and not in acquiescence to the Examiner's rejection, Applicant has cancelled claim 173. Accordingly, Applicant respectfully requests that the Examiner reconsider and withdraw the rejection.

Rejections under 35 U.S.C. § 102

The first 102 rejection

The Examiner has rejected claims 136, 137, 149, 150, and 171 under 35 U.S.C. § 102(e) as allegedly anticipated by Cantor *et al.* (U.S. Pat. No. 6,660,229 B2). The Examiner contends that Cantor *et al.* discloses a molecule that meets all of the limitations imposed by claims 136 and 137, embodiment (a)(i). Applicant respectfully traverses this rejection.

Applicant respectfully disagrees with the Examiner. Part (a)(i) requires a contiguous, self complementary sequence and an RNA binding site to which RNA polymerase can bind to form a transcription bubble. Cantor *et al.* does not disclose a sequence to which RNA polymerase can bind to form a transcription bubble. Rather, polymerization proceeds from the oligonucleotide by primer extension. In this situation, a transcription bubble is not formed.

Accordingly, Applicant respectfully requests that the Examiner reconsider and withdraw the rejection.

The second 102 rejection

The Examiner rejected claims 136, 137, 139-141, 149, 150, 171, and 174 under 35 U.S.C. 102(b) as allegedly anticipated by Berninger *et al.* (U.S. Patent No. 5,194,370). According to the Examiner, Berninger *et al.* disclose a proto-promoter construct comprising a self-complementary DNA sequence and an RNA-binding site, wherein said self-complementary sequence is made of one contiguous oligonucleotide to which RNA polymerase can bind, and having a 3' overhang that comprises 5 to 40 nucleotides. Applicant respectfully traverses this rejection.

Solely to advance prosecution, and not in acquiescence to the Examiner's rejection, Applicant has amended claim 136 to recite, *inter alia*, that when the abortive promoter cassette is that of part (a)(i), the target specific linker is not a nucleic acid. Applicant respectfully points out that Berninger *et al.* do not disclose a target specific linker that is not a nucleic acid.

Accordingly, Applicant respectfully requests that the Examiner reconsider and withdraw the rejection.

Rejection under 35 U.S.C. § 103

The first 103 rejection

The Examiner rejected claims 136, 137, 139-142, 144-156, 171, 172, and 174 as allegedly unpatentable over Munroe *et al.* in view of Berninger *et al.* (U.S. Patent No. 5,194,370). Applicant respectfully traverses these rejections.

Applicant disagrees with the Examiner's analysis. First, Applicant objects to the Examiner's citation to *In re Spada*, 15 USPQ2d 1655, 911 F2d 705 (Fed. Cir. 1990). See Office Action, page 7. The Examiner contends that "[s]o long as the prior art disclosure meets all of the limitations set forth in the product claims, said claims are anticipated and discovery of new property or use of previously known composition, even if unobvious from the prior art, cannot impart patentability to claims to a known composition." *Id.* Applicant contends that *In re Spada* is not appropriate to resolve patentability of Applicant's claims, as the Examiner has rejected the claims as obvious and not anticipated.

The gist of the Examiner's rejection is that a person skilled in the art would have been motivated to modify the bubble complex (as allegedly taught by Munroe *et al.*) with a target specific linker having a single stranded overhang region from 5 to 40 nucleotides (as allegedly taught by Berninger *et al.*). Munroe *et al.* describe that the nucleic acid fragments are ligated to an oligonucleotide by blunt-end ligation. *See* col. 2, lines 45-60. Blunt-ended nucleic acids do not have any nucleotide overhang. Moreover, modifying the bubble complex of Munroe *et al.* to create a bubble complex having a having a single stranded overhang region from 5 to 40 nucleotides would render the method of Munroe *et al.* nonfunctional for the reasons discussed below.

The goal of Munroe *et al.* is to provide a rapid method for efficient and representative amplification of genomic DNA from complex sources. See col. 1, lines 61-63. Munroe *et al.* discuss deficiencies in prior methods, such as interspersed repetitive element (IRE) PCR. See col. 1 of Munroe *et al.* Interspersed repetitive elements are elements of known sequence that occur frequently throughout the genome and include, for example, ALU repeats. In the IRE PCR procedure, intervening genomic sequence can be amplified by using primers that are specific for the repetitive element. *Id.* In this way, various regions of the genome can be amplified. However, Munroe *et al.* point out that "the utility of IRE PCR is further restricted by the apparent asymmetric distribution of repeat sequences within the genome" and this leads to "non-uniform distribution of IRE PCR products, leaving some regions of the genome under-represented." *Id.* To solve this problem, Munroe *et al.* sought to ligate genomic fragments with a bubble complex and use a bubble primer and a primer specific for a repetitive element to provide a rapid method for efficient and representative amplification of genomic DNA.

However, in order for the method to provide for efficient and representative amplification, it is clear that the genomic fragments to be ligated to the bubble complex should be of an average size that is suitable for amplification. It is known that PCR is very inefficient in the amplification of large fragments. Thus, if the average size of the ligated fragment is large, a rapid method for efficient and representative amplification of genomic DNA would not be achieved. Munroe *et al.* discuss that the preferred method for generating genomic fragments is digestion by restriction enzymes that have a 4 base pair recognition sequence and generally produce an average size fragment in the 300-

1000 base pair range. See col. 6, lines 36-39. Fragments of this size are easily amplified by PCR, and therefore, the amplified fragments would be representative of the genome.

There is no reason that would have prompted a person of ordinary skill in the art to ligate genomic fragments to a bubble complex having an overhang of 5 to 40 nucleotides, and therefore, there is no reason to make a bubble complex as claimed having an overhang of 5 to 40 nucleotides. As pointed out in Applicant's prior Amendment and Reply, type II restriction endonucleases are the most commonly used restriction enzymes and usually recognize 4-6-base pair (bp) sites on DNA and cleave each site in a separate reaction, however, these enzymes would not leave more than a 4 base pair overhang for subsequent ligation. There are a few type II restriction endonuclease recognizing an 8 base pair site, however, Bilcock *et al.* (*Journal of Biological Chemistry*, 274:36379-36386 (1999)) (previously submitted) demonstrate the unsuitability of these enzymes for use as restriction enzymes. Genomic fragments generated by an enzyme recognizing an 8 base pair sequence would not be of a suitable average size to allow for efficient and representative amplification of genomic DNA as required by Munroe *et al.* An 8 base pair recognition sequence would occur once every 4^8 base pairs. Thus, a restriction enzyme recognizing such sequence would generate fragments of an average size of 65,536 nucleotides. Fragments of such a large size could not be efficiently amplified by PCR. Consequently, it is clear that modifying the bubble complex to create a single stranded overhang region of from 5 to 40 nucleotides would render the method of Munroe *et al.* nonfunctional and would frustrate their purpose to "provide a rapid method for efficient and representative amplification of genomic DNA sequences." Accordingly, there is no reason to make a bubble complex having an overhang of 5 to 40 nucleotides and for at least these reasons, the Examiner

has not established a *prima facie* case of obviousness. Applicant respectfully submits that the Examiner's rejection, both the suggestion/motivation and reasonable expectation of success, is based on hindsight analysis in view of the Applicant's claimed invention.

Accordingly, Applicant respectfully requests that the Examiner reconsider and withdraw the rejection.

The second 103 rejection

The Examiner also rejected claims 151-156 and 162 under 35 U.S.C. § 103(a) as allegedly unpatentable over Berninger *et al.* in view of Kim *et al.* Applicant respectfully traverses this rejection.

Solely to advance prosecution, and not in acquiescence to the Examiner's rejection, Applicant has amended claim 136 to recite, *inter alia*, that when the abortive promoter cassette is that of part (a)(i), the target specific linker is not a nucleic acid. Applicant respectfully points out that Berninger *et al.* do not disclose or suggest a target specific linker that is not a nucleic acid.

Accordingly, Applicant respectfully requests that the Examiner reconsider and withdraw the rejection.

The third 103 rejection

The Examiner rejected claim 162 under 35 U.S.C. § 103(a) as allegedly unpatentable over Munroe *et al.* in view of Berninger *et al.*, as applied to claims 136, 137, 139-142, 144-156, 171, 172, and 174, and further in view of Kim *et al.* (U.S. Pat. No. 5,846,723). According to the Examiner, neither Munroe *et al.* nor Berninger *et al.* explicitly disclose that the linker be specific for a telomerase and Kim *et al.* disclose a

well known practice for detecting telomerase activities for the purpose of detecting malignant cancers. Applicant respectfully traverses this rejection.

Whether it would have been *prima facie* obvious to one of ordinary skill in the art to create a linker for the detection of telomerase is not material, because, as discussed above under "***The first 103(a) rejection***," the cited art does not provide any reason to make a bubble complex having an overhang of 5 to 40 nucleotides.

Accordingly, Applicant respectfully requests that the Examiner reconsider and withdraw the rejection.

Obviousness-type Double Patenting

The Examiner provisionally rejected claims 136, 137, 139-142, 144-148, 151-156, 162 and 171-173 for obviousness-type double patenting over various claims 23-31 and 35-43 of copending Application No. 10/976,240. The Examiner contends that the claims of the '240 application are drawn to a narrower species of the generic construct as claimed in the instant application. The Examiner contends that while claims 23-31 of the '240 application recite a generic term "abortive promoter cassette," in view of the figures of the '240 application referencing an abortive promoter cassette, the constructs are identical to the construct defined in the instant application, and therefore, deemed obvious over each other.

Applicant respectfully requests that the Examiner hold the present rejection in abeyance, pending the identification of otherwise allowable subject matter, at which time Applicant will consider filing any necessary terminal disclaimers.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicant therefore respectfully requests that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicant believes that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

Daniel J. Nevrivy
Agent for Applicant
Registration No. 59,118

Date: May 21, 2008

1100 New York Avenue, N.W.
Washington, D.C. 20005-3934
(202) 371-2600

663363_1.DOC